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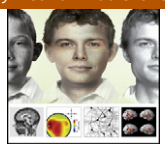

Review

Interactive Specialization: A domain-general framework for human functional brain development?

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ABSTRACT

A domain-general framework for interpreting data on human functional brain development is presented. Assumptions underlying the general theory and predictions derived from it are discussed. Developmental functional neuroimaging data from the domains of face processing, social cognition, word learning and reading, executive control, and brain resting states are used to assess these predictions. Finally, potential criticisms of the framework are addressed and challenges for the future presented.

Contents

1. Introduction

One of the fundamental questions in neurobiology concerns how different regions of the mammalian cerebral cortex develop their specificity. This question is particularly important for human cognitive neuroscience were regions of cortex collaboratively support "higher" cognitive

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functions not seen in most other mammals, and in which brain development is very prolonged continuing over the first two decades of postnatal life. This basic question in neurobiology underpins all human adult cognitive neuroscience studies in which particular cognitive functions are localized to areas of cortex, and is also of potential importance to future educational and clinical strategies. Further, relating evidence on the neuroanatomical development of the brain to the remarkable changes in motor, perceptual, and cognitive abilities during the first decade or so of a human life presents a considerable challenge of relevance to the new field of *developmental cognitive neuroscience*.

As a newly emerging field of science, developmental cognitive neuroscience can appear to students and experts alike as rather fragmentary, with different types of local hypotheses being used to motivate particular sets of studies, and domain or region-specific local theories being used to account for isolated islands of data (often from one lab). With rapid advances in the technology for tracing the genetic and neural basis of typical and atypical cognitive development, many intuitively surprising observations remain unexplained. How are we to come to understand these surprising observations, and to interpret and explain them within a broader context of other findings with different methods and populations?

Interdisciplinary fields such as developmental cognitive neuroscience face a formidable challenge in the development of adequate theories since scientists are required to construct theories that not only cross different levels of observation (such as genetic, neural and behavioural), but that also relate those different levels together in some coherent way. For a variety of reasons that I have discussed elsewhere (Johnson, in press), I suggest that developmental cognitive neuroscience theories should relate evidence from different levels of *observation* in terms of one level of *explanation*.

For several decades in the parent discipline field of cognitive development it was generally considered inappropriate to attempt to relate different levels of observation. Rather, the aim was to explain one level of observation (change in behaviour) in terms of one level of explanation (cognitive). This view was taken for a variety of reasons, but one influential source was the work of Marr (1982). Marr argued that, because the same computation can, in principle, be implemented on different computer or neural architectures, a computational account of cognition could, and should, be constructed independently from the details of its implementation on hardware. This influential argument led to the view that considering the role of the brain in cognitive development was reductionist in the sense that molecular and cellular processes could never provide an adequate explanation of cognitive processes.

While the case against an eliminative reductionist view (Churchland, 1986) is clearly correct, theories of biological development critically need to explain the reverse process (to reductionism) of the *emergence* of higher order structures of organization. Thus, while not denying Marr's anti-reductionist point, constructing a specific type of neural computer hardware will constrain the range of possible computations that could potentially be supported. With these considerations in mind, Mareschal et al. (2007), among others, argue that there are important constraints on computation imposed by its detailed implementation. Further, when attempting to bridge levels of explanation, mechanistic accounts of processes of computation and developmental change should be *consistent* across different levels, i.e. there is a need for isomorphism between levels of description. Since the overall goal of developmental cognitive neuroscience is to relate the genetic, neural, cognitive and behavioural accounts of human development, devising theories that specifically relate the different levels of observation seems crucial.

Theories come in different shapes and sizes. Specifically, the amount and range of developmental cognitive neuroscience data accounted for can independently vary along at least two dimensions: (a) how many levels of observation are incorporated or integrated, and (b) how domain-specific or domain-general (domain here is used in a general sense to refer to a facet of cognition) a theory is. It is a defining feature of developmental cognitive neuroscience, as opposed to traditional cognitive development, that multiple levels of observation are considered and related in terms of a single process or causal mechanism. One reason for this is that the parent discipline of cognitive development had been built on the strategy of explaining changes in behaviour during development in terms of cognition – a level of observation that is not itself directly observable. While the scientific strategy of theorizing at a level that is not directly observable is not unique to cognitive psychology, constraining theories of this kind by only one level of explanation is high-risk due to the lack of constraints it imposes.[1] In other words, a very wide variety of theories can successfully account for data at one level of observable only. For example, some of the same behavioural phenomena used to motivate arguments for the existence of "innate core knowledge" modules for geometric space and number can also be observed in day-old chicks and fish, as well as in human infants (Spelke and Kinzler, 2007). Given the radically different brains in these widely diverging species, it is evident that this kind of cognitive theory is not initally constrained by evidence about the underlying neural architecture.[2]

In cognitive neuroscience it is assumed that a better strategy is to sandwich a non-observable level of explanation between two levels of observable, such as those of brain and behaviour. With these considerations in mind, I have discussed different general theories of *functional brain development* designed to account for observable phenomena that underpin perceptual, motor, and cognitive processing (Johnson, 2001). These general theories are not intended to replace descriptions from cognitive models, or lower-level neural accounts, but rather to bridge the large gap that currently exists between cognitive theories and neural observations.

With regard to the second dimension of difference, theories in developmental cognitive neuroscience potentially

[1] Similar criticisms have been levelled at some theoretical claims in "evolutionary psychology".

[2] Albeit that corroborating evidence from neurophysiology is now being collected.

vary enormously in the scope of data that they account for from a single cognitive domain in a single population, to an account that crosses domains of cognition and populations (such as comparing typical and atypical development). Often, in biology the broader the scope of a theory, the less clearly it makes detailed domain-specific predictions. Thus, some have referred to such broad-scope theories as "frameworks" or "general theories". Put simply, frameworks are ways of thinking about, or viewpoints on, a large body of data (Morton and Frith, 1995). Frameworks have testable elements, but primarily serve as a coherent set of assumptions that, taken together, offer an account of a wide range of phenomena. In addition, within a framework more specific and detailed theories can be constructed. Further, general theories guide lines of research and the kinds of hypotheses that are explored.

In what follows I advance a domain-general framework for motivating and interpreting large bodies of data on the postnatal development of human brain functions. In previous publications I have presented different components of this framework (Johnson, 2000, 2001), focussed on applying it to specific domains of perception or cognition (Johnson et al., 2009), or to developmental disorders (Johnson et al., 2002). In the present paper I specifically focus on assessing evidence from developmental imaging across different domains of cognition, to ascertain the extent to which it can plausibly be considered as a candidate domain-general framework.

2. Three frameworks for understanding human functional brain development

Previous reviews of the literature in developmental cognitive neuroscience revealed that three different frameworks on human postnatal functional brain development are currently commonly adopted (Johnson, 2001). The first general theory that captures many implicit assumptions I have termed the *Maturational Viewpoint*. In general, the maturational viewpoint seeks to interpret emerging sensory, motor and cognitive functions in terms of the *maturation* of particular regions of the brain, usually specific areas of cerebral cortex. An area is said to be mature when it achieves the adult state of functioning, with any different state of functioning classified as being *immature*. An area reaching maturity is a one-off event, sometimes considered to have a sudden or non-linear onset (as opposed to the slower and more graded transitions attributed to learning) and to be caused by intrinsic genetic, biochemical, and/or neuroanatomical change.

Much of the research to date attempting to relate brain to behavioural development in humans has taken this approach. Evidence concerning the differential neuroanatomical development of brain regions should then predict the age when a particular region is likely to become functional. Conversely, success in a new behavioural task at given age is attributed to the maturation of a new brain region. Functional brain development is in this sense depicted as the reverse of adult neuropsychological studies of patients with brain damage, with specific brain regions being added-in during development (with the converse effects from being deleted by damage).

Despite the initial appeal of the maturational approach, it does not successfully explain many initially surprising observations on human functional brain development. For example, recent evidence suggests that some of the regions that are slowest to develop by neuroanatomical criteria (such as prefrontal cortex) can be activated from shortly after birth and appear to mediate cognitive functions even before they would be considered anatomically mature (for review see Johnson, 2011). Thus, the emergence of new behaviours is not necessarily linked to a previously immature, "silent" neural region becoming active when it matures. Another difficulty for the maturational viewpoint as a satisfactory explanation is that associations between neural and cognitive changes based on age of onset or transition are theoretically weak due to the great variety of neuroanatomical and neurochemical measures that change at different times in different regions of the brain. Thus, as the brain is continuously developing into adulthood, it is nearly always possible to find a potential neural correlate for any behavioural change in development. It is then tempting to jump to the assumption that this neural change *causes* the behavioural change in question. Finally, there is increasing evidence for neuronal changes caused through selective exchanges with the environment, and consequent experience-dependent plasticity.

A second general theory I have termed *Skill Learning*. Skill learning involves the proposal that the brain regions active in infants during the onset of new perceptual or motor abilities are similar, or even identical to, those involved in complex skill acquisition in adults. While the nature of the skills to be acquired change with development (from basic sensory and motor skills, to complex cognitive ones), the challenge to the brain at a given point in development may be equivalent. For example, Gauthier and Nelson (2001) speculate that development of face processing during infancy and childhood proceeds in a similar manner to acquisition of perceptual expertise for a novel visual category in adults. Similarly, prefrontal cortex may be more heavily engaged in simple tasks early in life (see later) due to its important role in skill acquisition. Different versions of skill acquisition propose different degrees of prespecification for the neural circuitry that underlies skill learning, with some proponents preferring to focus on inherent computational principles that maximise the brains ability to learn (for reviews see Spencer et al., 2009).

A third general theory is *Interactive Specialization* (IS) (Johnson, 2000, 2001). As reflected in its name, two key ideas underlie this approach. The first is the notion that during postnatal development changes in the response properties of some cortical regions occur as they interact and compete with each other to acquire their role in new computational abilities. From this perspective, some cortical regions begin with poorly defined and broad functionality, and consequently are partially activated in a wide range of different stimuli and task contexts. During development, activity-dependent interactions between regions sharpens up the functions and response properties of cortical regions such that their activity becomes restricted to a narrower set of circumstances (e.g. a region originally activated by a wide variety of visual objects, may come to confine its response to upright human faces). In other

words, some cortical regions become more specialized with development.[3] This process mirrors that known to occur at a cellular level during development, in which receptive or activity fields become increasingly fine-grained during development (e.g. Wills et al., 2010). The second aspect to Interactive Specialization is that postnatal functional brain development, at least within cerebral cortex, involves a process of organizing patterns of inter-regional interactions. According to this view, the response properties of a specific cortical region are partly determined by its patterns of connectivity to other regions, and their patterns of activity. The onset of new behavioural competencies during infancy will therefore be associated with changes in activity over several regions (networks), and not just by the onset of activity in one or more additional region(s).

3. Assumptions underlying Interactive Specialization

Elsewhere, I have discussed at length the different sets of key assumptions that underlie the three frameworks above (Johnson et al., 2002). Thus, for the present I will only briefly review assumptions critical for the IS theory that contrast with one or both of the other accounts.

- *Circular causality*: The IS framework adopts Gottlieb's "probabilistic epigenesis" view of development. Gottlieb (1992, 2007) distinguished between two approaches to the study of development, *deterministic epigenesis* in which it is assumed that there is a unidirectional causal path from genes to structural brain changes and then to psychological function, and *probabilistic epigenesis* in which interactions between genes, structural brain changes, and psychological function are viewed as bi-directional, dynamic and emergent. The latter has also been referred to as "circular causality" in recent literature. In contrast, deterministic epigenesis is a key feature of the maturational approach as defined here; region-specific gene expression is assumed to effect changes in intra-regional connectivity that, in turn, allows new functions to emerge. By this view, cause runs from gene to brain structure to brain function to behaviour.
- *Interactivity and brain networks*: This assumption of the IS approach is that the specialization of a cortical regions is determined within the context of its neighbours and connection patterns. In this respect, IS follows recent trends in the adult functional neuroimaging literature (Bressler and Menon, 2010) in which the response properties of a cortical region are determined by its patterns of connectivity to other regions as well as by their own current activity. Extending these ideas to development, the IS approach emphasizes that the emerging specialization of regions is influenced by changes in the inter-regional connectivity of the region in question. In contrast to this, explicit versions of the maturational view often appeal to neuroanatomical or neurochemical changes *intrinsic* to the region in question. Thus, the maturational view is more akin to a "mosaic" in which the developmental fate of each cortical region is independent of that of its neighbours (i.e. different and independent timetables for different regions), whereas in the IS framework region-region interactions are critical in determining developmental fate (Elman et al., 1996; Kingsbury and Finlay, 2001). The focus on interactions between regions is consistent with the emergence of networks to support cognitive functions, as opposed to the focus on the emergence of functionality in individual regions characteristic of the maturational approach (Kanwisher, 2010). Recent literature has also discriminated between the processes of *segregation* and *integration* in human functional brain development (Fair et al., 2007). Segregation may relate to the increased tuning within regions, whereas integration may result from the specialization of networks of regions (see later for discussion).
- *Self-organizing and activity-dependent process*: This assumption stands in stark contrast to the traditional view of functional brain development as the passive unfolding of a genetic blueprint or plan. The idea that biological development in complex organisms involves processes of self-organization is an old one (e.g. Waddington, 1975). When applied to functional brain development it suggests that the brain at one age may actively seek out the information it requires for its own further development, e.g. by directing sensory organs to slightly novel stimuli or environments. The assumption that human functional brain development is an activity-dependent process is also consistent with much evidence from developmental neuroscience (e.g. Stellwagen and Shatz, 2002). It is important to note that, even postnatally, the activity that shapes functional specialization can be intrinsic to the brain and is not necessarily directly evoked in response to environmental stimuli (see later discussion).
- *Dynamic mapping between brain and cognition*: A fourth underlying assumption concerns the mapping between cognitive functions and their neural substrate in the cortex. A necessary assumption within the maturational approach as presented here is that there is a one-to-one mapping between brain regions and particular cognitive functions, such that specific computations come "on-line" following the maturation of circuitry intrinsic to the corresponding cortical region. Similarly, explanations within a maturational approach depend on different cortical regions being assumed to have different maturational timetables, thus enabling new cognitive functions to emerge at different ages. In contrast the IS and skill learning frameworks assume a dynamic and changing mapping between cognitive functions and their neural substrate with development. When discussing functional imaging of developmental disorders, Johnson et al. (2002) point out that many laboratories have assumed that the relation between brain structure and cognitive function is unchanging during development. Specifically, in accord with the maturational view, when new structures come on line, the existing (already mature) regions continue to support the same functions they did at earlier developmental stages. This assumption is partly why it is acceptable to study developmental disorders in

[3] I note that the opposite process ("de-differentiation") may occur in later life aging.

adulthood and then extrapolate back in time to early development (Karmiloff-Smith, 2009). Contrary to this view, the IS approach suggests that when a new computation or skill is acquired, there is a re-organization of interactions between brain different structures and regions. This re-organization process could even change how previously acquired cognitive functions are represented in the brain. Thus, the same behaviour could potentially be supported by different neural substrates at different ages during development.

Stating that structure–function relations can change with development is all very well, but it lacks the specificity required to make all but the most general predictions. Fortunately, the view that there is competitive specialization of regions during development gives rise to expectations about the types of changes in structure–function relations that should be observed. These predications from the IS theory will be outlined and assessed in subsequent sections.

At this point it is important to acknowledge that some specific elements of the IS framework are related to other ideas and hypotheses that have been advanced in the field. For example, and in approximate chronological order, ideas relating selectionism to synaptic pruning (Kerszberg et al., 1992), hypotheses on the increasing localization of language areas (Neville et al., 1992), the "perceptual narrowing" hypothesis (Scott et al., 2007), and proposals about the increasing restriction of functional cortical areas with development (Durston et al., 2006). Interactive Specialization is also situated within a broader context of work on "neuroconstructivism" (Elman et al., 1996; Mareschal et al., 2007; Karmiloff-Smith, 2009).

4. Predictions and hypotheses

Frameworks are useful for a variety of reasons, but particularly so when they help to generate predictions that direct research (albeit that they will not always make opposing predictions), and when they offer coherent explanations of previously puzzling observations. Contrasting predictions derived from the three frameworks have been presented elsewhere (Johnson et al., 2002; Joseph et al., 2010), so for the present I will focus on predictions and interpretations offered by the IS view.

One set of predictions from the IS theory comes from the "Interactive" part, and another set from the "Specialization" part. To start with the latter, the hypothesized increase in specialization or tuning of activation of cortical regions has a number of consequences that generates testable predictions. I will refer to these as Hypothesis S1, S2, S3 and so on.

Hypothesis S1. Increased neural tuning or specialization in response to a given stimulus or set of tasks demands should be observable as a more selective (or narrow) response pattern. For example, unique ERP responses to specific stimuli (such as upright human faces) observed in adults will emerge during development from more broadly tuned responses that are initially elicited equally well by closely related stimuli (such as inverted or non-human faces) (de Haan et al., 2002).

Hypothesis S2. As a cortical region becomes more specialized (finely tuned) in its response properties it will respond less to non-preferred stimulus or task contexts. A consequence of this over many regions is that, for a given stimulus presentation or task context, we should observe a shrinkage or contraction of the extent of cortical tissue activated (Hypothesis S2a). However, this prediction will depend on the design of the functional imaging experiment in question, and particularly on what types of control conditions are subtracted or compared to the one of interest (see also, Joseph et al., 2010). If the experimental design and comparison conditions pose the question what cortical tissue is *sensitive* to a given stimulus or task context (e.g. by comparing to a general or unrelated baseline condition, such faces versus a fixation cross), the IS view predicts *shrinkage of the activated area* (Hypothesis S2a). In contrast, if the experimental design involves comparison of two closely related stimuli or conditions (e.g. by comparing faces to closely matched objects); the question being posed is what tissue is *selective* to that stimulus or task context. In this case, IS predicts the *emergence of response selective tissue* with age (e.g. tissue that selectively responds to faces more than closely matched objects) (Hypothesis S2b).[4]

Hypothesis S3. Changes in the degree of specialization (S1) for a given stimulus or task will directly correlate with changes in the degree of localization (S2) since, according to IS, they reflect the same underlying processes.

Hypothesis S4. Plasticity following brain damage or sensory deprivation will relate to the degree of functional specialization already achieved in a given region. A region that is already well specialized according to the criteria above will, according to IS, be less plastic in response to later life injury or deprivation. A region that is less specialized at a given age will have more options for future specialization (be more plastic).

Turning to predictions derived from the "Interactive" component of IS, several hypotheses derive from the view that the specialization of regions is influenced by the patterns of connectivity and the relative specializations, and current degree of specialization, of connectivity neighbours.

Hypothesis I1. During developmental change, neural activation profiles will rarely if ever change only in single regions. Rather, developmental change in cognitive skills or behaviour will be accompanied by widespread changes across multiple regions. Networks of regions will adjust the response properties of component regions to increase or optimise their overall functioning.

[4] Joseph et al. (2010) use a more complex taxonomy to characterise different levels of specificity of responses in cortical tissue. My usage of *stimulus-selective* corresponds to their categories of *preferential* and *selective* responding in relation to faces, i.e. a brain region shows a significantly greater response to faces than to other complex objects and a greater response relative to baseline. My usage of *stimulus-sensitive* corresponds to their categories of *conjoined* and *non-specific* in relation to faces, i.e. patterns of activation that do not meet the criteria for stimulus-selective (above) but where faces (or the stimulus in question) shows activation greater than baseline.

Hypothesis I2. The process of specialization will scale-up from regions to networks. The activation of networks of regions will, as a whole, become more selective to given stimulus or tasks contexts during development.

Hypothesis I3. The specialization of individual regions will be shaped by their involvement in one or more functional networks.

In the context of these hypotheses, I now review evidence, primarily from functional imaging studies, from several different domains in which the IS approach has been used to account for developmental change.

5. Face perception

Face perception has been a primary target domain for investigating issues about the emergence of specialization for a defined cortical function (Johnson et al., 2009; Cohen-Kadosh and Johnson, 2007; Kanwisher, 2010). From adult neuroimaging research we have an understanding of how and where faces are represented in the mature adult brain, including describing a "core" and "extended" network (Allison et al., 1994; Haxby et al., 1994, 2000). However, while we have some understanding of the neural substrate in adults, continuing debate focuses on the unresolved question whether face-sensitive cortical areas are unique for faces as a stimulus group ('domain specificity', Kanwisher, 2010; maturational framework), or whether such specialization is due to extensive perceptual training ('expertise approach', Gauthier and Nelson, 2001; skill learning framework). The IS framework potentially provides a mid-way account that involves both intrinsic and extrinsic factors, and predicts changes in both the degree of specialization and localization of face-evoked activity in cortex during development. Recently, several studies have used functional MRI to investigate face processing in children (for reviews see Cohen-Kadosh and Johnson, 2007; Joseph et al., 2010), and the majority of these studies have yielded support for the dynamic changes predicted by IS theory.

With regard to Hypothesis S1 (increased neural tuning or specialization in response to a given stimulus) several developmental fMRI studies have provided relevant evidence showing an increasing degree of tuning to faces in the core face network (e.g. Aylward et al., 2005; Gathers et al., 2004; Golarai et al., 2007; Scherf et al., 2007; Thomas et al., 2001; Joseph et al., 2010). For example, Gathers et al. (2004) with two groups of children (5–8, and 9–11 years) and adults showed that in spite of similar activation levels in the fusiform gyrus (FG) for the different age groups, only the 9–11-year olds show the commonly reported face-preferential, specialized responses in comparison to objects. Similarly, Aylward et al. (2005) compared the functional anatomy for faces versus houses in two different age groups (children aged 8–10 years, and 10–12 years) and found increased bilateral selective activation for faces in the older children in comparison to the younger children, a finding which correlated with the behavioural results. Hence, these fMRI studies support the notion that face processing becomes more specialized with increasing age (see de Haan et al., 2002 for converging evidence from ERPs).

Turning to Hypothesis S2, recall that if the experimental design and comparison conditions pose the question what cortical tissue is *sensitive* to a given stimulus or task context (e.g. by comparing to a general or unrelated baseline condition), the IS view predicts shrinkage of the activated area (Hypothesis S2a). In contrast, if the experimental design involves comparison of two closely related stimuli or conditions (e.g. by comparing faces to closely matched objects); the question being posed is what tissue is *selective* to that stimulus or task context. In this case, IS predicts the emergence of response selective tissue with age (e.g. tissue that selectively responds to faces more than closely matched objects; Hypothesis S2b). With regard to these localization hypotheses, most currently published studies[5] have found evidence for dynamic changes in the extent of cortical tissue activated between children and adults (e.g. Gathers et al., 2004; Golarai et al., 2007; Passarotti et al., 2003; Scherf et al., 2007), and at least three report the activation of additional areas that are not typically found in the mature adult brain, such as the left and right inferior frontal gyrus (Gathers et al., 2004; Passarotti et al., 2003; Joseph et al., 2010).

Of the studies mentioned above, two are of particular relevance as they specifically address *both* Hypotheses S1 and S2. Scherf et al. (2007) used naturalistic movies of faces, objects, buildings and navigation scenes in a passive viewing task with children (5–8 years), adolescents (11–14 years) and adults. They found that the children exhibited similar patterns of activation of the face-processing areas commonly reported in adults (such as the fusiform face area (FFA)). However, this activation was not selective for the category of face stimuli; the regions were equally strongly activated by objects and landscapes. Moreover, this lack of fine-tuning of classical face-processing areas stood in contrast to distinct preferential activation patterns for other object categories (occipital object areas and the parahippocampal place area). In a similar study, Golarai et al. (2007) tested children (7–11 years), adolescents (12–16 years) and adults with static object categories (faces, objects, places and scrambled abstract patterns). Consistent with Hypothesis S2b they found substantially larger right FFA and left parahippocampal volumes of selective activation in adults than in children.

Predictions derived from the IS approach as applied to the human face network have been most rigorously tested

[5] Not all developmental fMRI studies have reported changes in FFA during development as described in the main text. For example, Pelphrey et al. (2009) report adult-like responses in FFA, EBA, and the parahippocampal place area from ages 7 to 11 years. However, while an FFA was detectable in children, and voxels in that region showed the same degree of specificity seen in adults, many fewer voxels (around half) were classified as showing a face-selective response in children than in aduts (see also Cantlon et al., 2010). Thus, in accord with the results described in the main text, some evidence for an increase in the extent of face-selective tissue was provided. One currently unpublished study cited in secondary sources (Kanwisher, 2010), suggests that there may be no developmental change in the FFA when children from 5 years old are scanned using a number of different data acquisition and analysis methods that improve signal-to-noise ratio. However, it remains puzzling why neighbouring object-sensitive regions did not show similar developmental changes in all the previous studies – that also used a variety of different scanners, headcoils, and analytical methods.

by Joseph et al. (2010). In addition to their systematic confirmation of the predictions above (as compared to predictions from the maturational framework), these authors established that patterns of selective activation change across multiple regions in a way consistent with the whole network adjusting response properties of component regions to increase or optimise their overall functioning (Hypothesis I1). Cohen-Kadosh et al. (Submitted for publication) have explored whether the specialization process scales-up from regions to networks in the sense that the activation of networks becomes more selective to given stimulus or tasks contexts during development (Hypothesis I2). This was done by varying task demands while participants viewed an ongoing sequence of face stimuli that varied in identity, expression, or eye gaze (Cohen-Kadosh et al., 2010). These authors observed that the regions of the core face network became increasingly coordinated and integrated in their responses properties with development and, further, that the functional connectivity between regions of the network was modulated by task demands in adults, but was not in children. Thus, the selectivity of the response of the core face network as a whole only became selectively tuned to specific task demands later in development. Given the variety of different perceptual computations we perform on faces (expression, identity, eye gaze etc), they may be an ideal stimulus for exploring the specialization of network activation patterns in response to differing task demands.

Another area of face-processing research that could potentially contribute to our understanding of the developmental trajectory of face-specialized cortical areas is the work on developmental prosopagnosia. Developmental prosopagnosia refers to individuals who never develop typical adult face-processing abilities (Duchaine and Nakayama, 2006), and in particular facial identity recognition skills. This condition can occur in the absence of any obvious sensory or intellectual deficit (Avidan et al., 2005). Moreover, while there are cases of developmental prosopagnosia that arise from brain trauma early in life, there is increasing evidence for cases in which typical adult-like face-processing skills fail to develop in the absence of any known acquired injury (Duchaine and Nakayama, 2006). Functional MRI studies have generally shown that developmental prosopagnosics activate face-sensitive regions of cortex (for review see Duchaine and Nakayama, 2006). However, the degree of selectivity of this response remains in doubt, and a plausible interpretation of these results is that while adult developmental prosopagnosics show activation in face-sensitive regions, they may also show the lack of specificity in this response reported earlier for typically developing children. Moreover, Avidan et al. (2005) showed using fMRI that in four developmental prosopagnosics face perception recruited additional brain areas (e.g. the inferior frontal gyrus) that were not commonly found in typical adults. Interestingly however, inferior frontal gyrus activation has been observed in children in several of the developmental neuroimaging studies reported above (Scherf et al., 2007; Passarotti et al., 2003, 2007; Gathers et al., 2004). Thus, predictions from IS accounts for data from developmental prosopagnosia in terms of delayed or impaired specialization process.

If this account of developmental prosopagnosia is correct then with sufficient training on faces the selectivity of the response of cortical areas, and their inter-connectivity, should change toward the typical adult pattern. This was tested in a training study with a developmental prosopagnosic that showed that as behavioural performance improved the selectivity of cortical processing of faces (as measured by the N170 component) increased (DeGutis et al., 2007). Further, these authors also observed increased functional connectivity between face-selective regions as measured by fMRI, particularly the right occipital face area and the right fusiform face area. In short, the functional anatomy and behavioural abilities exhibited by developmental prosopagnosics are reminiscent of the findings obtained in developmental neuroimaging studies (see above), in which children exhibit neural activity for faces in the brain areas typically found adults, but this activation, while less reliably localized is also still far from being face-specialized. Further studies on both adults and children suffering from developmental prosopagnosia will be needed to shed light on this issue.

6. The social brain and social cognition

Beyond face perception and the core face network, other regions in what has become known as the social brain network are thought to help support more complex aspects of social perception and cognition. Another cortical area known to respond to social stimuli, and also implicated in social perception, is the Superior Temporal Suclus (STS) (Allison et al., 2000). In adults, the response properties of portions of the STS are highly specific. For example, while STS responds to moving biological stimuli, it does not respond as well to non-biological similar moving stimuli, or to static pictures of biological stimuli (Puce et al., 1998). In addition, several frontal and prefrontal areas are also known to be activated during social cognition computations (Frith and Frith, 1999, 2006). In particular, there are now several fMRI studies with children of various ages using different tasks showing that medial prefrontal cortex (MPFC) is consistently activated when children engage in mentalizing or other aspects of human social interaction (Blakemore et al., 2007; Kobayashi et al., 2007; Ohnishi et al., 2004; Pfeifer et al., 2007; Wang et al., 2006). Can these developmental changes be interpreted within the IS framework?

In relation to Hypothesis S1 (increased neural tuning or specialization) developmental neuroimaging studies show that STS can be activated by dynamic social stimuli from at least mid-childhood (Mosconi et al., 2005), and probably even during infancy (Lloyd-Fox et al., 2009). The observation that regions that will become part of the adult social brain are activated by social stimuli in a broadly tuned way from early in life is entirely consistent with the IS theory. While the degree of specialization of the STS response during infancy remains to be determined, Carter and Pelphrey (2006) used fMRI to test the specificity of response of the STS and other regions in 7- and 10-year old children while they viewed a variety of biological motion and related stimuli (such as walking robots). They observed that, consistent with Hypothesis S1, the STS became increasingly specific in

its response properties to biological motion with increasing age. While research on the STS is clearly not as advanced as that on the FFA, the evidence currently available indicates that similar processes of emerging functional specialization may occur.

With regard to dynamic changes in the spatial extent of cortical regions activated in response to social cognition (Hypothesis S2), in all of the currently published developmental studies of MPFC, children recruited MPFC more extensively than adults when engaged in mentalizing tasks, even when task performance and possible baseline differences were controlled for (see Johnson et al., 2009 for review). For example, Wang et al. (2006) employed an irony task to investigate the comprehension of communicative intentions from cartoons in adults and children (9–14 years), and found that children recruited MPFC and left inferior frontal gyrus to a greater extent than adults, whereas adults recruited the FG, extrastriate areas and the amygdala more strongly than children. Furthermore in a correlation analysis the authors showed that, within the group of children, there was a positive correlation between age and FG activity and a negative correlation of age with extent of MPFC activity. Similarly, Blakemore et al. (2007) reported that adolescent participants (12–18 years) when thinking about intentions showed more extensive activity in MPFC than adults, whereas adults activated parts of the right STS more than adolescents. Two other developmental mentalizing studies available revealed very similar patterns of findings. Pfeifer et al. (2007) examined brain activity during self-knowledge retrieval and found that 10-year-old children engaged MPFC to a greater extent than did adults. Kobayashi et al. (2007) presented adults and children (8–11 years) with theory of mind tasks and also reported that the children showed more activity in MPFC than adults, but that adults exhibited great activity in the right amygdala than children. Taken together, these studies consistently show that with age the extent of MPFC activation during mentalizing tasks becomes more focal, whereas activity in posterior (temporal) cortical areas sometimes increases.

While currently there have been no systematic investigations of changing patterns of selective activation across multiple brain regions, Hypotheses I1 is clearly supported by evidence from MPFC studies showing that while the extent of activation decreases with development in late childhood resulting in the focal selective activation of specialized sub-regions of MPFC in adults, there is also a corresponding increase in the extent of activation in more posterior regions such as FFA and STS. Thus, the networks of regions composing the social brain are likely to be adapting their functionality within the context of a whole emerging network. Clearly, only further studies, or appropriate re-analyses of existing data, can definitively address this issue.

7. Word learning, reading, and visual word-form system

Infants tend to initially learn words relatively slowly, but at about 18–20 months infants typically show a rapid increase in the production of words, often called the vocabulary spurt or the naming explosion. Some researchers have speculated that this sudden increased ability is correlated with changes in organization of language-relevant brain regions (Mills et al., 1993). One study used ERPs to investigate the neural correlates of processing of known and unknown words in children before and after the vocabulary spurt. The results showed that before the vocabulary spurt, the amplitudes of ERPs from 200 to 400 ms were larger to known than unknown words. These ERP differences were broadly distributed over anterior and posterior regions of both the left and right hemispheres. In contrast, for 20-month olds, who had vocabularies over 150 words, ERP differences from 200 to 400 ms were more focally distributed over temporal and parietal regions of the left hemisphere. A subsequent analysis that compared children with different vocabulary sizes but with age held constant showed that this shift in brain response was more directly related to vocabulary than to age. These results, and those of similar studies, are consistent with Hypothesis S2 in that they show a more focal pattern of activation with increasing age and experience.

Another aspect of language processing in the brain that involves experience is learning to read. Reading involves linking the visual word form with the sound structure of language and interpreting its meaning. The development of reading poses a somewhat different challenge than the development of the ability to perceive and produce spoken language. Unlike the latter abilities, which seem to unfold without special effort as children develop, reading is a relatively recent development in human history that is acquired through explicit teaching and much practice. In this way, studying the acquisition of reading provides an interesting opportunity for investigating how experience impacts brain function during development.

One set of brain areas that have been intensively studied in this respect is the 'visual word-form system' (VWFS). The visual word-form system in adults is within the left occipto-temporal cortex, centred on the mid-fusiform gyrus, and shows a tuned response to visual word forms compared to other complex visual stimuli. The VWFS appears to be involved in perceptual expertise for word recognition that allows words to be perceived and processed quickly and automatically in skilled readers (e.g. Brem et al., 2010).

Important changes have been observed in activation of the VWFS over the years when children begin to learn to read. In a recent review, Schlaggar and McCandliss (2007) used the IS framework to interpret wide-ranging evidence on the neural changes associated with learning to read. Summarising the results from several developmental fMRI studies they state: "Developmental functional imaging results from several groups are beginning to converge on a central conclusion regarding developmental changes in extrastriate regions involved in reading. During the ages when reading skill is acquired, a transition occurs from bilateral extrastriate region involvement for reading to a predominance of left (relative to right) ventral occipito-temporal cortex involvement. This finding was evident in several large cross-sectional developmental fMRI studies of reading-related tasks (Schlaggar et al., 2002; Shaywitz et al., 2004; Brown et al., 2005) described above. Additionally,

Eden and co-workers (Turkeltaub et al., 2003) reported a similar pattern in their large cross-sectional developmental fMRI study that related age and various measures of linguistic skill to activation elicited by an implicit reading task. They showed an age-related decline in right extrastriate activity, whereas homologous left cortical regions maintained their level of activity across age groups". The changes summarised by Schlaggar and McCandliss (2007) clearly provide support for Hypothesis S2a in that they show a transition to more focal patterns of specialized tissue with experience and development, although closer analysis of the different comparisons and conditions employed in these studies is obviously required. Again, the changes in VWFS occur within a context of changes in patterns of activation (such as those in the right hemisphere), providing at least preliminary support for Hypothesis I1.

The dynamic changes in the extent of cortical tissue activated in response to visual word forms can also be observed with other imaging methods. For example, ERP studies have also been employed to investigate the development of the VWFS, as this region is believed to contribute to the N170 ERP component elicited by visual words. In adults, the N170 for visual words is left lateralised, and this spatial distribution of the response is believed to be a signature of perceptual expertise of visual words as opposed to other forms of perceptual expertise (e.g. for faces; Maurer et al., 2008). Preschoolers' N170's for words are slow and do not show sensitivity to words or letters (Maurer et al., 2005); however after a year and a half of reading instruction, reading fluency correlated with the degree to which the N170 showed an adult-like response (Maurer et al., 2006). Overall, these findings provide convergent evidence for the idea that perceptual expertise for recognising visual words involves a process whereby brain occipito-temporal brain activity elicited to words becomes more specific to words (Hypothesis S1) and more focalized to the left hemisphere (Hypothesis S2).

Schlaggar and McCandliss (2007) conclude their review of the neural basis of learning to read by saying "these findings converge to support the notion that the development of fluent word recognition is systematically related to functional refinements in early perceptual processes. These novel perceptual abilities, which are triggered during the first few hundred ms of processing a visual word, undergo considerable experience-dependent refinement manifest as more focal, left-lateralized patterns as reading experience develops". The process described is clearly consistent with the IS framework.

Very recent studies have reinforced and amplified this conclusion. For example, Bitan et al. (2009) examined the developmental changes in interactions among brain regions while children performed rhyming judgements on visually presented words. The authors interpret their results in terms of the increasing influence of frontal regions over temporal cortical areas in the left hemisphere. In older, but not younger, children top–down control processes mediated by frontal structures may selectively enhance the sensitivity of lateral temporal cortex to input information from the fusiform gyrus. This discovery is highly consistent with Hypotheses I1 and I2 in that it shows the gradual emergence of a coordinated and specialized network of regions. In another recent study, Brem et al. (2010) collected both MRI and ERP data from children in the context of a reading skills training study. They demonstrated that the learning of letter-speech sound correspondences in young non-reading children results in the emergence of cortical tissue sensitive to words (as opposed to false fonts) in occipital-temporal cortex. Print-selective activation emerged as a direct of result of training in the areas that will later become the adult VWFS (as measured by fMRI) and in an N200 component of the ERP. This study illustrates that at certain points in development even relatively brief training (in this case 3–4 h) can initiate the specialization processes hypothesized by the IS framework (Hypothesis S1).

8. Prefrontal cortex and executive control

One of the first areas to be explored in developmental fMRI studies was the prefrontal cortex and its associated executive control functions. For example, Casey et al. (1997) and Thomas et al. (1999) administered a "go/no-go" task to assess inhibitory control and frontal lobe function to healthy volunteers from 7 years of age to adult. The task involved participants responding to a number of letters, but withholding their response to a rarely occurring "X". More than twice the volume of prefrontal cortex activity (dorsolateral prefrontal cortex) was observed in children compared to adults. One explanation of this finding is that children found the task more difficult and demanding than adults. However, children with error rates similar to those in adults showed some of the largest volumes of prefrontal activity suggesting that task difficulty was not the important factor. These findings are clearly puzzling when viewed from the context of the maturational framework, but are consistent with Hypothesis S2 discussed earlier.

Evidence in support of Hypothesis S2 has been the explicit topic of debate within this domain. Durston et al. (2006) marshalled evidence from several developmental fMRI studies of prefrontal cortex activation consistent with a shift from "diffuse to focal" cortical activity during development. Specifically, in a combined longitudinal and cross-sectional study they observed attenuated activity in dorsolateral prefrontal cortical areas, in addition to increased focal activation in ventral prefrontal regions that was related to performance in a target detection task. In this study the authors dissociated the extent of cortical tissue activated (whole-brain analyses) from the changes in activation amplitude (ROI analyses), and observed a developmental and performance-related trend from widespread lower activation to more focal but greater activation. These changes seem entirely consistent with a tuning process in which one region increasingly becomes increasingly specialized for a specific computation to the exclusion of others.

Hypothesis I1 (developmental change in cognitive skills or behaviour will be accompanied widespread changes across multiple regions) has also been explicitly addressed in the domain of cognitive control. For example, Luna et al. (2001) tested participants aged 8–30 years in an oculomotor response-suppression task to see which regions "matured" over this age period. Their behavioural results

showed that the adult level of ability to inhibit prepotent responses developed gradually through childhood and adolescence. The difference between pro-saccade and anti-saccade conditions were investigated with functional MRI, and revealed dynamic changing patterns of brain activation during development. Both children and adolescents had reduced amplitude of activation compared to adults in some cortical areas (superior frontal eye fields, intra-parietal sulcus), and also in several sub-cortical areas. However, both children and adolescents also had activation in regions not found to show differences in adults. For example, children displayed increased relative activation in the supramarginal gyrus compared to the other age groups, and the adolescents showed greater differential activity in the doroslateral prefrontal cortex than children or adults. These findings illustrate the widespread network changes in the neural basis of behaviour over developmental time, with different patterns of activation being evident at different ages.

Another example of the development of prefrontal activation patterns during childhood comes from studies of verbal fluency tasks in which participants are asked to generate words in response to a cue (e.g. to generate examples of a target category, or generate a verb that relates to a cued noun). Several studies have shown that adults and school age children (Hertz-Pannier et al., 1997; Gaillard et al., 2000) typically activate left hemisphere frontal cortical networks including Broca's area, premotor, prefrontal and supplementary motor areas as well as, less consistently, temporal cortical areas including superior temporal, middle temporal and supramarginal gyri. In addition, some degree of activation in homologous right frontal regions is almost always found both in adults (Pujol et al., 1999; Springer et al., 1999) and in children (Hertz-Pannier et al., 1997; Gaillard et al., 2000). Two studies have found that both the degree to which activation is bilateral (rather than left dominant) and the extent of this activation is greater in children than in adults (Gaillard et al., 2000; Holland et al., 2001). Thus, as in the other examples discussed above, typical development is associated with a reduction in the extent of activation of cortical areas and, as a consequence, an increased lateralisation of activation to the left hemisphere with age (Hypothesis S2).

9. Resting-state networks and spontaneous activity

To this point the majority of the examples we have discussed have involved research on the emergence of specialized functions in human cortex in specific regions such as the FFA or VWFS. However, several of the predictions from the IS viewpoint refer to our understanding of how *networks* involving different regions, each with their own different specializations, emerge (Hypotheses I1–3). In other words, while we have some good examples of functional brain development at the level of individual cortical regions, we are still largely in the dark about how the larger scale of cortical function in terms of networks of regions develops (Johnson and Munakata, 2005; Stevens, 2009). Some recent studies have sought to address this issue by examining resting-state networks during development. While data from resting-state networks cannot be used to make direct inferences about specialization in response to task contexts, functional resting states are thought to reflect recent experience as well as being constrained by the current neuroanatomy (for review see Uddin et al., 2010).

One example of this line of work comes from Fair et al. (2007, 2009) who used functional connectivity analyses in fMRI to study resting state "control" networks in school age children and adults. Their analysis allows them to infer the nature and strength of functional connections between 39 different cortical regions. They found that development entailed both segregation (i.e. decreased short-range connectivity) and integration (i.e. increased long-range connectivity) of brain regions that contribute to a functional network. In a similar study, the general developmental transition from more local functional connectivity to greater and stronger long-range network connectivity was confirmed using slightly different methods and 90 different cortical and sub-cortical regions (Supekar et al., 2009).

Assuming that the process underlying resting activity mirror to some extent those during recent task-dependent activation, the decrease in short-range inter-regional functional connectivity is readily explicable in terms of the IS view. As neighbouring regions of cortical tissue become increasingly specialized for different functions (e.g. faces versus objects), they will less commonly be co-activated. This process may also involve synaptic pruning and has been simulated in neural network models of cortex in which nodes with similar response properties cluster together spatially distinct from nodes with other response properties (e.g. Oliver et al., 1996). Thus, decreasing degrees of functional connectivity between neighbouring areas of cortex is readily predicted by models implementing principles of the IS view (see also Cantlon et al., 2010).

More challenging to the IS framework is to account for the increase in long-range functional connections. A maturational explanation of the increase in long-range functional connectivity would suggest that this increase is due to the establishment or strengthening of the relevant fibre bundles. However, the increase in functional connectivity during development may occur after the relevant long-range fibre bundles are in place (see Fair et al., 2009; Supekar et al., 2009 for discussion) suggesting that we still require an account of why functional connectivity may expand from local to long-range.

One proposal is that the strengthening and maintenance of long-range brain connections is at least partially an activity-dependent aspect of brain development reflecting networks of regions that are commonly co-activated in specific task contexts. This raises the question of why and how do particular anatomically distant brain regions begin to cooperate in a functional network? A speculative answer to this question may lie in scaling up the basic mechanisms of Hebbian learning. It may be that regions that tend to be co-activated in a frequently encountered task context strengthen or maintain the connections between them. While each region is becoming individually specialized for a particular function, this intra-region change in specialization is modulated and influenced by its presence within an emerging network of co-activated structures. For

example, in a task that requires visually guided action, a variety of visual and motor areas will be co-activated along with multi-modal integration areas. If the task is repeated sufficiently often then these patterns of functional co-activation will be strengthened, and the specialization of individual regions forming the network will proceed within this context of overall patterns of activation. These established patterns of functional co-activation may then become incorporated into resting-state networks (Lewis et al., 2009; Uddin et al., 2010) which themselves influence the patterns of activation observed in subsequent tasks (Zhang et al., 2009). Thus, commonly encountered task contexts, such as face-to-face social interaction with another human, may induce increasingly embedded and specialized patterns of network activation.

Another reason why anatomically distant regions may strengthen and maintain their connectivity relates to the fact that most of the long-range functional connections studied by Fair et al. (2007) involved links to parts of the prefrontal cortex. This part of the cortex is generally considered to have a special role during development in childhood and skill acquisition in adults (Thatcher, 1992; Gilbert and Sigman, 2007). Indeed, PFC may play a role in orchestrating the collective functional organization of other cortical regions during development (see Section 10).

10. Discussion

In the previous sections I have illustrated the potential of the IS framework to explain dynamic changes in cortical activation patterns in a domain-general way. As stated earlier, this will not remove the need for more detailed domain-specific theories to be developed within the framework. I now consider some other areas and domains in which the IS framework could potentially be applied over the next few years, but where there is currently a paucity of relevant data. Then I will go on to review some challenges and caveats to the IS framework, before closing with some proposals for future directions.

It will be evident to most readers that the IS framework has implications broader than the typical development of human brain functions, and some of these implications have already been explored in considerable detail elsewhere (Johnson et al., 2002). The key points are that some developmental disorders can be characterised as having delayed processes of specialization (resulting in more widespread and less stimulus or task-specific patterns of cortical activation), or as having atypical patterns of specialization (tuning cortical areas to stimuli or tasks in ways that differ from the typical pattern). An example of the former comes from some studies of developmental prosopagnosia, which was discussed earlier. An example of the latter may be the residual atypical associations symptomatic of synaesthesia (Cohen-Kadosh et al., 2009).

There seems little doubt that the IS framework could be applied to domains other than those discussed earlier (see Johnson, 2011). Among several candidate domains is that of number. One view of the acquisition of number skills is that during infancy numbers do not have a unique representation (Rips et al., 2008), and other non-numerical dimensions, separately or jointly, can serve as cues in order to detect changes in quantity/magnitude. A likely reason for this might be a shared magnitude mechanism for non-numerical dimensions such as size, density, time, that precedes neurons that are specialized for numerical magnitude (Walsh, 2003). In this scenario, different magnitudes, possibly also including numbers, are jointly represented from infancy (Cohen Kadosh and Walsh, 2008; Feigenson, 2007). Later, in development, there is a hypothesized increase in the specialization of the neural tissue underlying computations for numbers, leading to the emergence of specifically tuned neuronal circuits for numerical magnitude (Cohen Kadosh and Walsh, 2008). This view of the emergence of number systems in the brain is consistent with some emerging evidence from developmental imaging. While regions responsive to number may be activated from 4 years old or earlier (Cantlon et al., 2006), left fusiform regions that are selective to letters in adults are equally activated by numbers in 4–5-year old children (Cantlon et al., 2010). This suggests that numbers and letters may have much more overlapping neural processing prior to significant education. Such emerging findings are, at least in general terms, consistent with the IS framework, and seem worthy of more detailed investigation in the future.

10.1. Challenges and caveats

Some have suggested that patterns of shrinkage of cortical activation could be artefacts of functional methods and/or analyses. For example, some activation maps that include more errors in task performance show a qualitatively greater spatial extent of activation and lower peak signal magnitudes (Brown et al., 2006). While such factors could account for the results from some individual studies, the large number of functional MRI studies from different labs, in different domains, with different data acquisition and analysis methods, and including some studies matching for behavioural performance across age, make any single methodological explanation unlikely. Further, converging results have been obtained with other methods, such as ERP, making it even more unlikely that one, or a few, methodological factors account for these trends in the data.

Another potential criticism is of the IS framework itself, rather than the supporting data. This criticism is that subsets of the results described above are also consistent with either the maturational or skill learning frameworks. For example, the emergence of face-selective cortical tissue during childhood could also be consistent with a maturational view in which it is argued that region-specific gene expression changes the intrinsic connectivity of FFA, or its biochemical milieu, to enable adult functioning. Joseph et al. (2010) have addressed this issue in considerable detail arguing that while the maturational view predicts increases in the extent of stimulus or task-specific tissue, only the IS framework also predicts shrinkage of stimulus or task sensitive tissue in the context of network-wide adjustments to functioning. This illustrates the status of IS as a framework or general theory which generates a series of predictions, only a sub-set of which will discriminate it from other frameworks or perspectives. As discussed

earlier, it is the overall scope and breadth of data that it accounts for that will ultimately determine its success. Having said this, additional data can often help discriminate between the frameworks outlined earlier. To return to the example of the emergence of stimulus-selective cortical tissue with experience or development, the maturational and IS frameworks make different predictions about the functional state of an area preceding its change to become stimulus-selective (see also Joseph et al., 2010, their Table 1). The IS framework predicts that an area will become increasingly specialized for a function, and thus will go from being more broadly tuned, and responsive to the stimulus in question, to more narrowly tuned and responding to the given stimulus only. In contrast, according to the maturational view it is possible that an area not previously sensitive to a given stimulus could mature directly to selectively responding to that stimulus. The prediction from the IS framework has been confirmed for face processing (Joseph et al., 2010).

As stated in Section 1, the IS framework is intended as potentially a domain-general framework for interpreting a variety of data on the emergence of human brain functions. A potential criticism of this approach is that different functional areas in the cortex may arise due to quite different neurodevelopmental mechanisms. For example, Kanwisher (2010) argues that while the visual word-form area may emerge developmentally through mechanisms akin to those described in this paper, the FFA arises because "the specific instructions for constructing the critical circuits for face perception are in the genome". In other words, different functionally defined cortical areas (even corresponding areas in the two hemispheres) result from fundamentally different neurodevelopmental factors. In contrast to this view, many developmental neuroscience studies suggest a vast majority of common basic mechanisms of neural plasticity and representation across large extents of cortex (for review see Kingsbury and Finlay, 2001), albeit with possible differences in the timing of developmental events. Clearly, only further research will resolve these matters.

Anticipating another source of potential criticism, the traditional nature–nurture debate continues to polarise discussion in some domains of cognitive and language development. With its emphasis on activity-dependent processes of change, the IS framework may be perceived by some as supporting empiricist or learning accounts of developmental change, in contrast to those who argue for the maturation of innate modules. While the IS framework undoubtedly has different underlying assumptions, and some different predictions, from the maturational framework, an emphasis on activity-dependent specialization does not directly equate to experience-driven learning. As we saw in the previous section on resting states, intrinsic brain activity may be a greatly underestimated source of functional activity that could potentially help sculpt emerging connectivity patterns during development. This intrinsic activity of the brain remains poorly understood, but is likely to reflect both the brains current state of connectivity and its recent history of functional activity.

A related criticism of the IS framework is the claim that it assumes that all cortical areas are equipotential, and that this is implausible. Although, as stated earlier, the IS framework assumes that inter-regional connections are as important as intrinsic connectivity in determining a regions functionality, this does not mean that all cortical regions start with equal potential. According to the IS view, small-scale areas of cortex become tuned for certain functions as a result of a combination of factors, including (i) the suitability or otherwise of the biases within the large-scale region (e.g. transmitter types and levels, synaptic density, etc.), (ii) the information within the sensory inputs (sometimes partly determined by other brain systems), and (iii) competitive interactions with neighbouring regions (so that functions are not duplicated). In addition to these constraints, particular regions appear to be situated within a context of connectivity that gives them a greater influence over emerging functionality in other regions. As mentioned earlier, the prefrontal cortex is generally considered to have a special role during development in childhood and skill acquisition in adults (Thatcher, 1992; Gilbert and Sigman, 2007). Johnson (2011) reviewed a number of studies consistent with the idea that PFC may play a role in orchestrating the collective functional organization of other cortical regions during development.

10.2. Future directions

The putative role of the PFC in constraining emerging functions in other regions illustrates a future challenge for the development of the IS framework. To date, most examples of how regions interact and compete to acquire functions have involved *horizontal* interactions between regions at approximately equivalent stages of neural computation. However, it seems evident that similar principles apply to *vertical* interactions within the brain where one structure provides top–down feedback to influence the emergence of functionality in another (Stevens, 2009). In this regard, analyses of resting-state functional connectivity have shown that adult networks have a more hierarchical structure that is optimally connected to support top–down relations between one part of the network and another (Supekar et al., 2009).

One of the features of a hierarchical network is the capacity for one region to feedback highly processed sensory or motor input to the earlier stages of processing. In much the same way as we hypothesized that lateral inter-regional interactions help shape the intrinsic connectivity of areas to result in functional specialization, interactions between regions connected by feedback and feedforward connections may also help shape the functional specialization of the areas involved. Top–down effects play an important role in sensory information processing in the adult brain (e.g. Siegel et al., 2000). For example, during perception, information propagates through the visual processing hierarchy from primary sensory areas to higher cortical regions, while feedback connections convey information in the reverse direction. In a neurocomputational model of feedback in visual processing in the adult brain, Spratling and Johnson (2004) demonstrated that a number of different phenomena associated with visual attention, figure/ground segmentation, and contextual cueing could all be accounted for by a common mechanism underlying

cortical feedback. Extending these ideas to development, there are potentially two important implications of feedback that will benefit from future exploration. The first of these will be to examine how the specialization of early sensory areas is shaped by top–down feedback, and vice versa, during development. The second topic for investigation will be to examine the consequences of relatively noisy or poor quality cortical feedback in the immature cortex.

Finally, it will be evident that some of the predictions of the IS framework presented earlier are yet to be seriously tested, and all of them still require thorough assessment in different domains (e.g. S3, S4). In particular, relating changes in neuroanatomical measures of connectivity to functional changes will be critical for the detailed confirmation of the general theory presented here.

11. Conclusions

A framework for interpreting and guiding research on human functional brain development has been presented. While not all predictions made by the general theory are unique, when assessed as a whole over a number of different domains the predictions are largely upheld by current data. Most importantly, the framework potentially provides a structured agenda for future research, and allows for generation of domain-specific theories within it.

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